Case scenario 1
Clinical Breakout Session

Smallpox Vaccine Adverse Event Workshop

January 22-23, 2003

CASE #1 – Progressive Vaccinia

- 43yo Male nurse presents for take check on day 7 following smallpox vaccination. He appears well and his only complaint on ROS is a mild headache and fatigue. Removal of his vaccination site bandage reveals an ulcerative lesion measuring approximately 2.5 cm on a non-erythematous base with scant non-bloody discharge. Due to your concern regarding the ulcerative presentation and size of the central vaccination lesion, you arrange for a site re-check in 2-3 days.
- The patient fails to keep his scheduled follow-up appointment because he was not concerned and was feeling well. Instead, he left town to visit friends. Feeling guilty about missing his appointment, he presents to the clinic on day 14 following smallpox vaccination. His ROS is unremarkable and he appears well.

CASE #1 – Progressive Vaccinia

- On examination, the central ulcerative lesion now measures 5 cm. The edge of the lesion has necrotic changes, while the uninvolved skin shows no signs of inflammation. There are no exudates present. There is no evidence of maceration and the patient admits that he has not been covering the lesion because he ran out of bandaging supplies while on vacation
- **Vax Hx:** Flu '01, Td '93, routine childhood immunizations including smallpox vaccine but no scar is detected.
- **PMHx:** Cellulitis following needle stick in 1998 which required hospitalization for IV antibiotics, PPD 0x0mm '02
- **Meds:** Herbals, occasional aspirin
- **SH:** Single, surgical nurse supervisor, heavy smoker

CASE #1 – Progressive Vaccinia

1. **How do you chart his "take"?**
   Major reaction
2. **Is this an adverse reaction?**
   yes
3. **If so; what is your vaccinial AE differential diagnosis?**
   Severe take
   Early progressive vaccinia (suspect underlying immunocompromised condition)
4. **What is your level of concern for vaccinial adverse reaction on Day 7 and Day 14 post-vaccination?**
   Day 7 – moderate concern (severe take vs. PV)
   Day 14 – significant concern for PV given continue extension, lack of pain and inflammation.

CASE #1 – Progressive Vaccinia

- *See Clinical Evaluation Tools' (CET) description of PV → Although this patient was evaluated on day 14 post-vaccination, he meets the CET criteria for "suspected PV" due to the rapid, progressive and painless extension of the central lesion.*
- *Index of suspicion for immunocompromised or immunodeficient conditions. Probe for history for risk factors or symptoms to help make a clinical diagnosis:*
  - *HIV - needle stick, sexual history, IV drug use, transfusions*
  - *Cancer – recurrent infections, constitutional symptoms, easy bruising, headache, nonspecific cough.*

Progressive Vaccinia

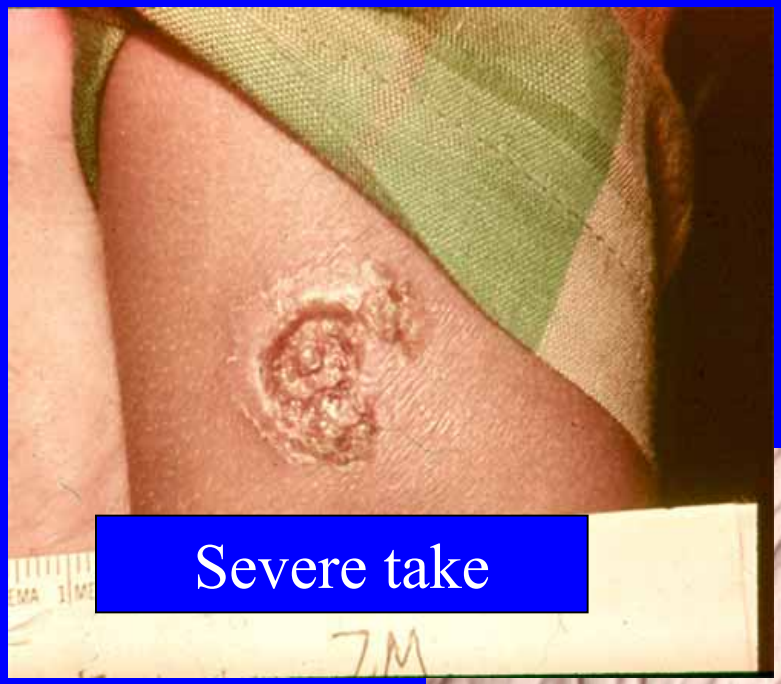
- Rapid, progressive and painless extension of central vaccination lesion OR progression without apparent healing after 15 days
- Virus continues to spread locally and through viremia (metastatic lesions to skin, viscera and bone)
- Initially little or no inflammation at the site and generally little pain
- Bacterial superinfection may develop later

Progressive Vaccinia

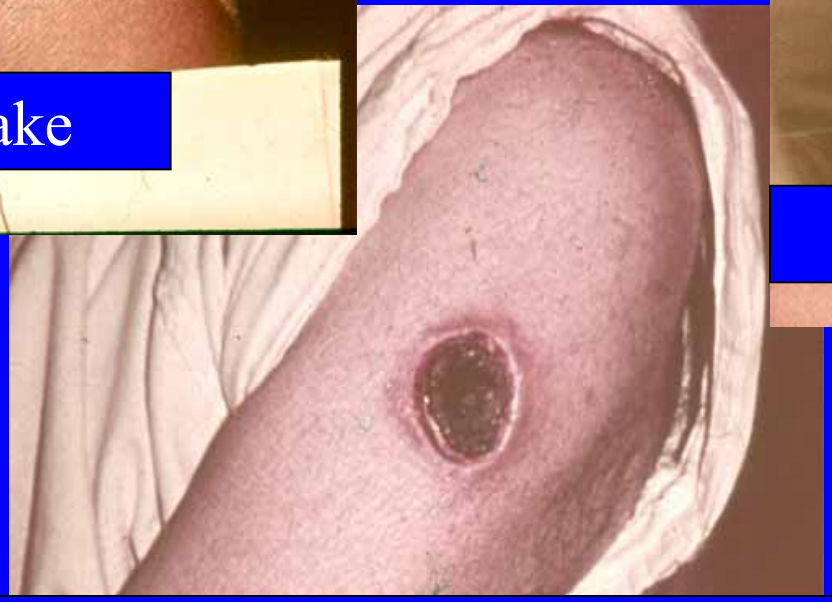
- Occurs almost exclusively among persons with cellular immunodeficiency
- Can occur in persons with humoral immunodeficiency
- Can occur following revaccination of people who have become immunosuppressed since their primary vaccination

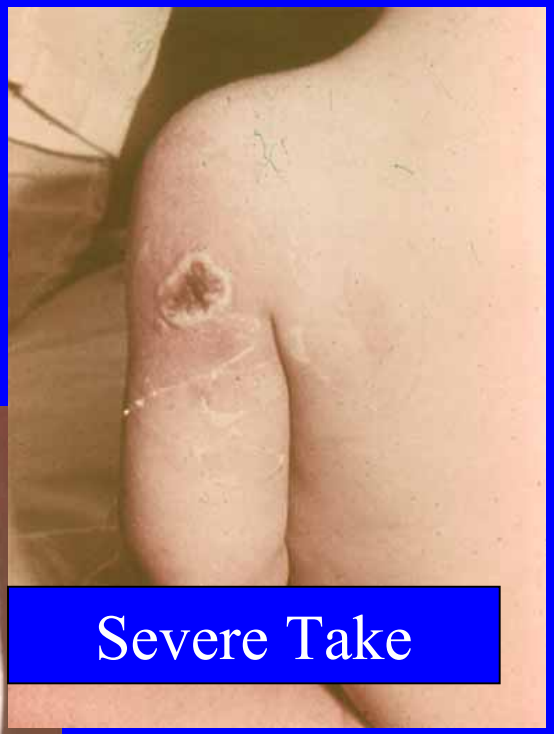
Progressive Vaccinia: Prognosis

- Protective T-cell count level and humoral immunity unknown although anecdotal reports of poorer prognosis with CMI deficits
- Better prognosis if immunosuppression is reversible (e.g. systemic steroid use)



Severe take





Severe Take

Atypical PV in 64yo with lymphoma and IgA, IgM and IgA deficiency

Photo credit: J. Michael Lane, MD MPH

CDC Teaching slide set Adverse reactions following smallpox vaccination

Progressive Vaccinia vs. Severe Take

- Distinguishing features of severe take:
  - Resolves in 1-2 weeks w/o therapy
  - Has signs and symptoms of inflammatory response
  - Pain is present
  - Lesion does not rapidly extend
  - Absence of metastatic lesions
  - Occurs in immunocompetent host

PV: Differential Diagnosis

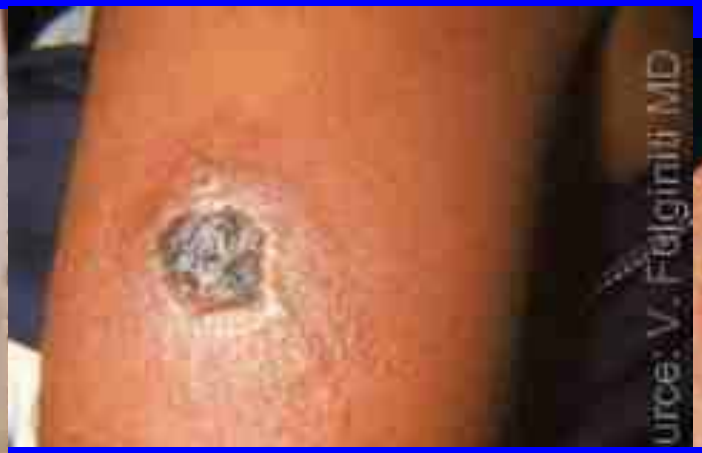
- Ulcerative take
- Severe bacterial infection
- Severe chickenpox
- Disseminated herpes simples
- Other necrotic conditions

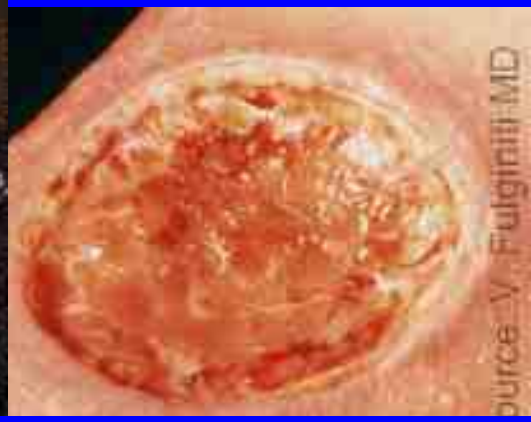
Progressive vaccinia with metastatic lesions in adult with CLL

Photo credit: J. Michael Lane, MD MPH

CDC Teaching slide set Adverse reactions following smallpox vaccination

SCID





Lymphoma and PV

Lymphosarcoma

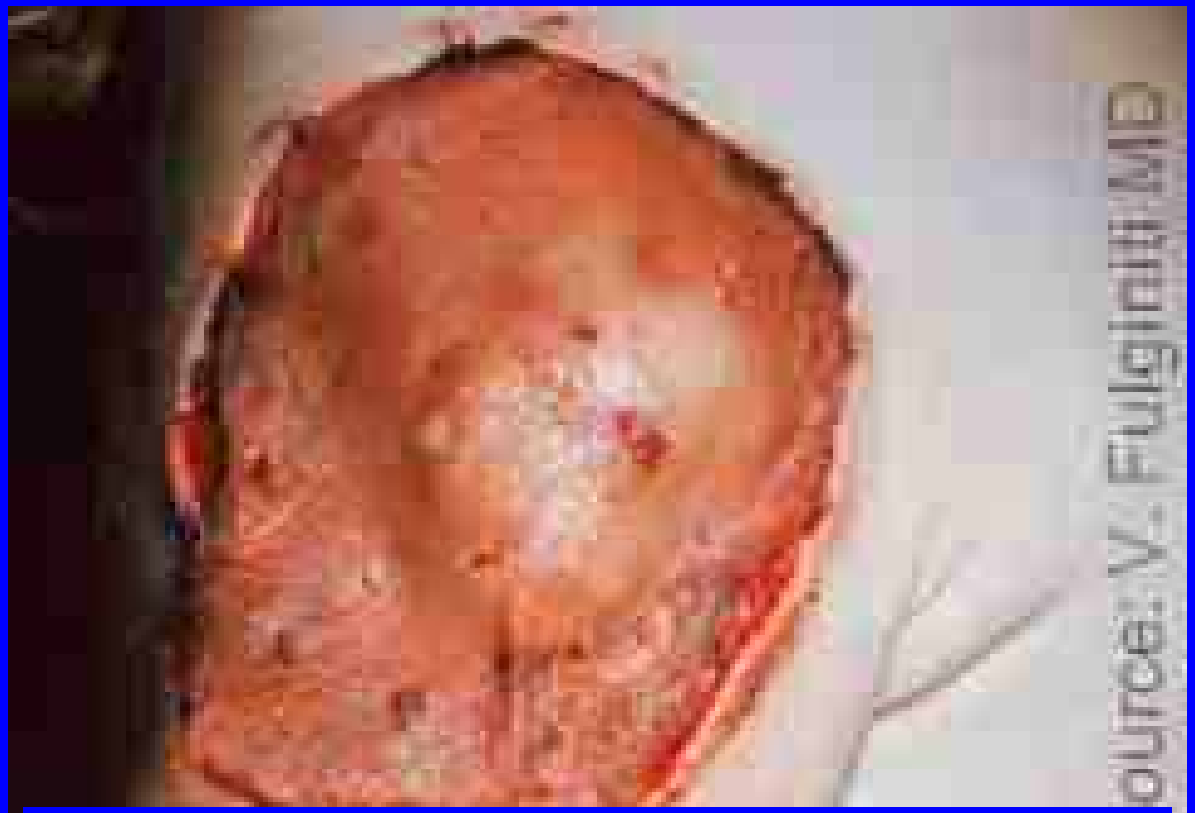
Hypogammaglobulinemia

Progressive vaccinia

Photo credit: V. Fulginiti, MD and Logical Images

http://www.bt.cdc.gov/training/smallpoxvaccine/reactions/default.htm

CDC Immunization



Child with absent
cell-mediated immune function

Progressive vaccinia

Photo credit: V. Fulginiti, MD and Logical Images

http://www.bt.cdc.gov/training/smallpoxvaccine/reactions/default.htm

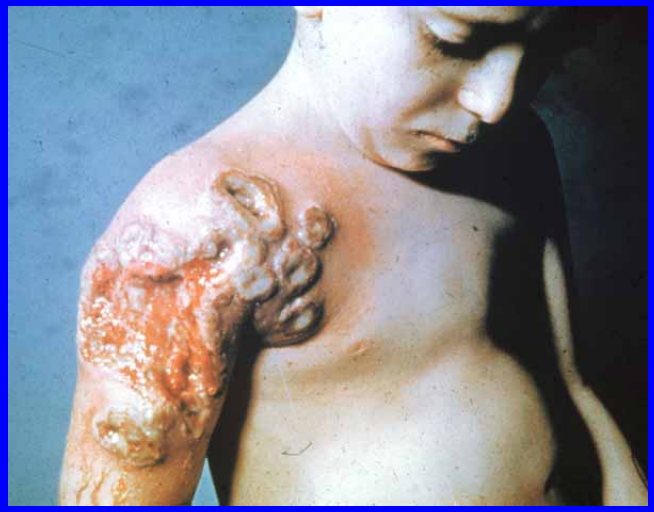
Progressive Vaccinia

- Requires aggressive therapy with VIG
- Newer antivirals not studied in humans. Cidofovir second-line agent
- Surgical debridement used in past with variable success
- Anticipate high mortality rate despite modern advances in medical care
- Lesions contain vaccinia virus: Infection control precautions

CASE #1 – Progressive Vaccinia

5. What in features of the history or exam help you draw this conclusion?

- *Absence of erythema and other inflammatory changes*
- *Painless presentation*
- *Ulcerative changes*
- *Initial size and continued progression*
- *Lack of systemic symptoms*



CASE #1 – Progressive Vaccinia

6. **How likely do you think that non-vaccinial etiologies might be contributing to the presenting symptoms?**
   - *Unlikely – why?*
7. **If this patient did not give a history of smallpox vaccination, what would be your non-vaccinial differential diagnosis?**
   - Bacterial superinfection (e.g., ecthyma)
   - Anthrax
   - Arthropod bite with necrosis

CASE #1 – Progressive Vaccinia

8. What are your next steps for clinical evaluation?

- Repeat history
- Complete physical exam
- Basic labs – (CBC/diff)
- Immunological work-up (CD4 count, quantitative immunoglobulins, other?)
- Special labs (HIV w/consent)
- Site culture.
- Biopsy for bacterial, fungal and viral culture. EM to rule out presence of Orthopoxviruses. Evaluation for malignant changes. Special studies as indicated.**9.**

CASE #1 – Progressive Vaccinia

9. Is this a case that you would like to have further consultation?

- Yes

10. Should a VAERS form be completed? If so, who should fill it out?

- A VAERS form should be completed but should NOT delay reporting to the appropriate Local/State Health Department officials or CDC.
- CDC will assist in completing the VAERS form for this case.
- Reporting criteria: all clinically significant adverse reactions following smallpox vaccination.
  - Serious or unexpected adverse events which require consultation or consideration of VIG/cidofovir administration→ contact local/state Health Department officials AND CDC immediately.
  - Serious or unexpected and does NOT require consultation or use of VIG/cidofovir. → Report within 48 hours to VAERS.
  - All other adverse events→ within one week.

CASE #1 – Progressive Vaccinia

11. If so, who do you call? And what is your request?
- Locally assigned hospital clinician, with referral to infectious disease or dermatologist specialist.
- Local / State Health Department official
- CDC's Clinician Information Line to request consultation and VIG release (Cidofovir is second-line IND therapeutic).

12. What is the prognosis for this condition?
- *High mortality rate (~100%) prior to the introduction of VIG. Mortality was significantly reduced following the introduction of VIG and older antivirals (~20%).*

13. What are the considerations for infection control measures? Should this patient continue in his clinical duties.

CASE #1 – Progressive Vaccinia

BREAKOUT QUESTONS:

1. The patient is found to be HIV+, what is your prognosis? Would your prognosis be different if the patient was newly diagnosed with chronic myeloid leukemia (CML)?

   It appears that the type of immunodeficiency correlates with the prognosis for of PV. Anecdotal experience suggests that despite treatment with VIG, persons with cell-mediated immune deficits have a poorer prognosis than those with humoral deficits (Fenner). It is likely that the degree and type of immunocompromised correlates with the risk of rogressive vaccinia, although the protective level of T-cell count or humoral immunity is unknown.

CASE #1 – Progressive Vaccinia

BREAKOUT QUESTONS:

2. Consider a patient who discloses HIV status AFTER vaccination but does NOT have an adverse reaction. What would you do?

Presently there is no indication for prophylactic use of VIG/Cidofovir under IND in an individual with contraindication to vaccination (e.g., pregnancy, eczema/atopic dermatitis or other immunocompromised condition) that is inadvertently exposed to vaccinia (either through vaccination or close contact. You should report these cases to your local/state health department official and the CDC for inclusion in the CDC Inadvertent Exposure Registry (call 1-877-554-4625). If an adverse reaction develops in these cases, the CDC is available for consultation and to facilitate expedited release of VIG/cidofovir as clinically indicated.

CASE #1 – Progressive Vaccinia

- **DISCUSSION POINTS**
- Despite screening tools, there will most likely be inadvertent vaccination of individuals with contraindications. Therefore, for each case that present with adverse reactions and probe for a history of risk factors (see *top yellow* box on Clinical Evaluation Tools)
- Adverse Reactions following smallpox vaccination are a CLINICAL diagnosis. Use of VIG should NOT be delayed in a patient with severe adverse reactions such as PV, EV (with extensive lesions or with systemic illness) or GV (severe form). Do not delay administering VIG while awaiting confirmation of the suspected underlying immunocompromising condition(s) (e.g., HIV, Cancer or other immunodeficiencies)
- Consider avoidance of ASA in viral infections due to theoretical risk of Reye's syndrome

CASE #1 – Progressive Vaccinia

- GOALS:

1. Clinical picture of PV spectrum with compare and contrast to a “severe ulcerative take”.
2. Therapeutic modalities available and appropriate indications.
3. Understand the historical experience with PV prognosis in patients with immunodeficiencies (e.g., humoral versus cell-mediated immunity)
4. Reporting criteria and timeline.

CASE #1 – Progressive Vaccinia

VAERS online reporting demonstration